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Comprehensive first-line magnetic resonance imaging in hypertension: Experience from a single centre tertiary referral clinic

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Abstract

European guidelines recommend that patients with hypertension are assessed for asymptomatic organ damage and secondary causes. We propose that a single magnetic resonance imaging (MRI) scan can provide comprehensive first-line imaging of patients assessed via a specialist hypertension clinic.

200 patients (56% male, aged 51 ± 15 years, office BP 168 ± 30 / 96 ± 16 mmHg) underwent MRI of the heart, kidneys, renal arteries, adrenals and aorta. Comparisons were made with other imaging modalities where available. 61% had left ventricular hypertrophy (LVH), 14% reduced ejection fraction and 15 patients had myocardial infarcts. Echocardiography over-diagnosed LVH in 15% and missed LVH in 14%. Secondary causes were identified in 14.5% of patients: 12 adrenal masses, 10 renal artery stenoses, 7 thyroid abnormalities, 1 aortic coarctation, 1 enlarged pituitary gland, 1 polycystic kidney disease, 1 renal coloboma syndrome.

Our comprehensive MRI protocol is an effective method of screening for asymptomatic organ damage and secondary causes of hypertension.

Introduction

Hypertension is a global health problem; at least a quarter of the adult population has high blood pressure (BP) and the world-wide prevalence is predicted to rise to 1.56 billion by 2025(1). The 2013 European Society of Hypertension / European Society of Cardiology guidelines for the management of arterial hypertension recommend that all patients with high BP are investigated for asymptomatic target organ damage to enable evaluation of their cardiovascular risk, and thus guide the initiation of appropriate treatment(2). Initial assessment with a 12-lead electrocardiogram (ECG) and basic biochemical tests is advised as standard for all patients, with guidance that additional testing should be performed if indicated by history or examination findings(2). Investigation for secondary causes of hypertension is recommended where there is clinical suspicion(2). In the United Kingdom, the 2011 National Institute for Health and Care Excellence guideline on the diagnosis and management of hypertension in adults also recommends additional investigation in patients at higher risk of secondary hypertension, specifically including those with young onset hypertension (<40 years old), treatment resistant hypertension, rapidly worsening or accelerated hypertension, or in those with history or examination findings that might indicate a secondary cause(3).

In this study we aimed to establish the utility of magnetic resonance imaging (MRI) as a screening tool in hypertension in patients assessed via a specialist hypertension clinic. The European guidelines acknowledge the value of cardiac MRI, but recommend echocardiography and peripheral arterial/abdominal ultrasound as first line imaging modalities (2). However, as MRI becomes increasingly available, it is likely to prove a useful tool in the assessment of patients. For example, cardiac MRI (CMR) is **widely regarded as the gold standard non-invasive imaging modality for the clinical assessment of** left ventricular mass (LVM) and left ventricular hypertrophy (LVH)(4), and additionally, MRI techniques can be used to image the vasculature (including the renal arteries), renal parenchyma and adrenal glands with high accuracy(5, 6). MRI could improve diagnostic

efficiency in these patients as it is a highly sensitive imaging modality and would avoid the need for multiple appointments for echocardiography, renal ultrasound and, potentially, vascular computed tomography (CT) angiography.

We propose that a single MRI scan could provide all of the routine imaging required for the evaluation of both target organ damage and the identification of potential secondary causes in patients in the context of a tertiary hypertension service.

Methods

Study population

This was a retrospective analysis of 200 consecutive patients assessed with a hypertension protocol MRI scan, from a prospectively gathered clinical database of patients investigated at a tertiary hypertension clinic (Bristol Heart Institute, University Hospitals Bristol NHS Foundation Trust).

Eligible study participants were those referred for MRI as part of their standard clinical hypertension work-up between November 2010 and July 2015, and includes patients with young onset hypertension (yHTN, onset <40yrs), drug resistant hypertension (rHTN, BP >140/90 mmHg despite ≥ 3 anti-hypertensive medications), uncontrolled hypertension (ucHTN, BP >140/90 mmHg on <3 anti-hypertensives), and other difficult to treat hypertension (e.g. accelerated hypertension, highly labile hypertension or hypertension with disproportionate target organ damage).

Baseline demographics and clinical characteristics were recorded. Patient height and weight were measured with calculation of body mass index (BMI). A BMI ≥ 30kg/m² was defined as obesity(7).

Office systolic (SBP) and diastolic blood pressures (DBP) were measured in the seated position using

a standard oscillometric device and appropriately sized cuff, taking the mean of at least two repeat readings, where available.

To assess the reliability of our MRI findings, results were compared with the clinical reports from previous echocardiographic, renal ultrasound or renal CT angiographic studies performed as part of each participant's hypertension assessment. Likewise, results from CT scans performed as part of any additional evaluation for patients with positive findings on MRI were also reviewed.

The local research ethics committee confirmed that the study conformed to the governance arrangements for research ethics committees (REC). The study was conducted with the patients' written consent. The study was performed in accordance with the declaration of Helsinki.

MRI protocol

Images were acquired from the level of the Circle of Willis to the level of the femoral heads.

CMR was performed at 1.5 Tesla (Avanto, Siemens, Erlangen, Germany). Steady-state free precession short-axis whole LV cines (8 mm slice thickness, no slice gap, temporal resolution 38.1 ms, echo time 1.07 ms, representative field-of-view (FOV) in-plane pixel size 1.5×0.8 mm) were used for the estimation of LV mass and volumes. Myocardial replacement fibrosis was assessed by late gadolinium enhancement (LGE)(8). An inversion-recovery fast gradient-echo sequence was performed 10–15 min after intravenous administration of 0.1 mmol/kg gadobutrol (Gadovist, Bayer Pharma AG, Germany), in two phase-encoding directions where there was potential artefact. Tailored inversion times were used in each patient to null normal reference myocardium.

Renovascular assessment consisted of Time-resolved angiography With Interleaved Stochastic Trajectories (TWIST) contrast enhanced magnetic resonance angiography (MRA), which creates multi-phase, multi-planar images of the thoracic and abdominal vasculature; angiography was analysed using multiplanar reformatting post-processing software (cmr42; Circle Cardiovascular Imaging Inc., Calgary, AB, Canada). Axial T1-weighted images through the abdomen and pelvis with 5mm slice thickness were also performed.

CMR analysis

The assessment of left ventricular volumes and LVM were performed as described previously(9). Briefly, endocardial contours were defined at end-diastole and end-systole on the LV short-axis stack using blood pool/endocardial border threshold detection software (cmr42; Circle Cardiovascular Imaging Inc., Calgary, AB, Canada), which has been previously validated(10). Epicardial contours were defined manually at end diastole. The LVM was estimated by multiplying the total myocardial volume, including papillary muscles and LV trabeculations (equivalent to LV dry weight), by 1.05 g/ml, which is the specific gravity of myocardium, as described previously(9). The LVM was indexed to body surface area, calculated using the Mosteller formula. Ejection fraction was calculated from the end-diastolic and end-systolic endocardial volumes, and long axis function was assessed using mitral and tricuspid annular plane systolic excursion.

LVH was defined as indexed LVM >95th percentile of established CMR reference ranges indexed to body surface area (men: <35 years, >87 g/m²; ≥35 years, >78 g/m² and women: <35 years, >71 g/m²; ≥35 years, >70g/m²)(11). LV remodelling was defined as a ventricle with normal indexed LVM but elevated LV mass/volume ratio (M/V)(12). An increased M/V was defined as >95th gender-specific percentile (men: >1.12 g/ml and women:>1.14 g/ml) from healthy volunteers, as described previously(12). The presence of LGE was quantified by visual analysis.

Statistical analysis

Statistical analysis was performed using GraphPad Prism (La Jolla, CA, USA). All data presented as mean \pm standard deviation. The chi-squared test was used to compare categorical data. A Kruskal-Wallis test was used to compare non-parametric data, with Dunn's multiple comparison test between groups. Significance was taken as $p < 0.05$.

Results

Demographic data

Data from two hundred consecutive patients from our specialist hypertension clinic who underwent MRI as the imaging component of their assessment for target organ damage and potential secondary causes of hypertension are presented. 38% of patients had drug resistant hypertension, 32% had young onset hypertension, 18% had uncontrolled hypertension, and 12% had other difficult to treat hypertension. Patient demographic data is shown in Table 1. There were no adverse events as a result of the MRI scans; however one scan was abandoned due to claustrophobia. All patients except one (renal coloboma syndrome) had an eGFR of >30 ml/min/1.73m².

Target organ damage detected by MRI

Overall, 79% (157/200) of patients had evidence of target organ damage. The proportion of patients with target organ damage differed between the four hypertension subgroups (see Table 2, $p < 0.0001$); 92% (70/76) of patients with rHTN, 59% (38/64) with yHTN, 89% (31/35) with ucHTN and 72% (18/25) with other HTN.

In this study cohort, 61% (122/200) of patients had LVH and 7% (13/200) had left ventricular remodeling without hypertrophy. An example of left ventricular hypertrophy is shown in Figure 1A.

Late gadolinium enhancement demonstrated left ventricular replacement fibrosis in 15% (30/200) of patients; the 15 patients with a non-infarction pattern of LGE all had mild patchy intramyocardial enhancement. Based on the nature of their LVH, characteristic basal mid-wall fibrosis and others markers, four patients were reclassified with probable hypertrophic cardiomyopathy (see example in Figure 1B)(13, 14). From a functional perspective, 14% (27/200) of patients had reduced ejection fraction and 42% (84/200) had impaired long-axis function. There was a difference in LVM between hypertension groups (see Table 1, $p<0.01$) with a significant difference between those with rHTN and yHTN on subgroup analysis ($p<0.05$). Viewed as the proportion of patients in each hypertension subgroup with LVH, there was also a significant difference between groups (see Table 2, $p<0.0001$); LVH in 74% (56/76) of those with rHTN, 38% (24/64) of those with yHTN, 74% (26/35) with ucHTN and 64% (16/25) with other HTN.

We identified 15 (7.5%) individuals with evidence of a previous myocardial infarction, seen as sub-endocardial scarring in a coronary artery distribution on late gadolinium enhancement (see Figure 1C&D); in 5 of these patients this was a novel diagnosis. 44 patients (22%) had an ectatic aorta (surgical intervention not indicated) and six patients had evidence of significant pre-existing cerebral or peripheral vascular disease and were on secondary prevention medication.

Secondary causes of hypertension identified by MRI scanning

29 patients (14.5%) had potential secondary causes of hypertension identified on MRI. There was a difference in the proportion of patients with a potential secondary cause on imaging between the hypertension subgroups (see Table 2, $p=0.04$); secondary causes were identified in 17% (13/76) of those with rHTN, 6% (4/64) of those with yHTN, 23% (8/35) of those with ucHTN and 28% (7/25) with other hypertension. In the full cohort, we identified 12 patients with adrenal masses/hyperplasia (including two reported as pheochromocytomas), 10 with renal artery stenoses (RAS), 6 with renal abnormalities potentially causing secondary hypertension (4 renal atrophy, 1

polycystic kidney disease, one renal coloboma syndrome), 7 with thyroid abnormalities, one individual with aortic coarctation, and one with an enlarged pituitary gland (some patients had more than one pathology identified). 27% of patients had ≥ 1 accessory renal artery. See Table 3 for details, examples are shown in Figure 2. It should also be noted that 47% of the study patients were obese, however, when comparing those with and without obesity, a similar proportion of patients had another potential secondary cause of hypertension identified on MRI in this cohort (13/93 (14%) vs 26/107 (15%), $p=ns$).

MRI versus other imaging modalities

MRI results were compared with conventional echocardiographic, renal ultrasound or CT scans performed as part of a participant's hypertension assessment, where available. In this cohort, 84 patients had had previous echocardiograms, 81 had had renal ultrasound, and 11 patients had CT imaging (adrenal protocol CT or renal CT angiography) either prior to their MRI scan or as part of more focused investigation of their MRI findings.

When compared to CMR, echocardiography over-diagnosed LVH in 15% (false positive) and missed LVH in 14% (false negative). Echocardiography had a sensitivity of 79% and specificity of 64% for the detection of LVH in this dataset (see Supplementary Table 1 for predictive values). Simple renal ultrasound assessment failed to detect four cases of RAS. One patient who had 'normal' adrenal glands reported on MRI had a 6mm adenoma identified on subsequent focused adrenal CT imaging, which was performed due to positive biochemistry indicating Conn's syndrome; this was retrospectively not visible on the initial MRI. In another case, an adrenal mass was reported as a likely pheochromocytomas on MRI, but was felt to be benign following endocrine testing and a dedicated adrenal CT (see Table 3). Following initial investigation with MRI, further imaging was recommended in 24/200 patients; this included focused CT to further characterize renal artery

stenoses and adrenal masses, ultrasound of thyroid abnormalities (all benign except an MEN2a case), or imaging of other incidental findings.

Discussion

We have shown that MRI is a safe and effective imaging strategy for evaluating target organ damage and screening for secondary causes in patients assessed within the context of a specialist hypertension clinic. MRI has the significant benefit of being able to image multiple systems in one session, and is a low risk investigation that does not involve ionizing radiation; this is particularly relevant when investigating patients with young onset disease who may go on to have repeated imaging during their lifetimes. The high prevalence of pathology seen in this study justifies the use of more advanced imaging techniques in higher risk/more complex patients with hypertension as recommended by European guidelines(2).

Asymptomatic target organ damage was identified in over three quarters of our study population, and most notably, LVH was demonstrated in 61% of the patients. The prevalence of target organ damage and LVH differed between the subgroups of hypertensive patients in this study. Fewer patients with young onset hypertension had LVH, and whilst this may reflect the fact that these patients have been exposed to high BP for a shorter period of time, the development of different hypertensive heart disease phenotypes is likely to be multifactorial (15). The level of left ventricular hypertrophy across the full study cohort is higher than the 36-41% prevalence seen in the general hypertensive population(16), however, we present data for those requiring assessment in a tertiary clinic. Target organ damage is highly prevalent in established HTN (echocardiographic LVH seen in 55-75% of patients with rHTN (17)), and healthcare professionals should have a low threshold to request further imaging in these individuals, particularly if this will alter management due to increased cardiovascular risk.

In this cohort there was also a relatively high (14.5%) prevalence of potential secondary causes of hypertension compared with the 5-10% rate of secondary hypertension reported amongst general hypertensive populations (18-20). Once parallel biochemical testing is taken into account, the prevalence of secondary hypertension seen in this study cohort may be more consistent with rates of secondary hypertension of 20-31% seen in patients with more severe or treatment resistant hypertension(21, 22).

There was a significant difference between the prevalence of secondary causes between the subgroups of hypertensive patients in this study. The highest prevalence of secondary causes was in the 'other' hypertension group; this reflects the nature of the patients in this group, some of whom were referred to the clinic for additional assessment of known secondary hypertension. However, it is interesting that fewer of those with yHTN had possible evidence of secondary hypertension compared with the other groups. It might have been expected that yHTN patients would be more likely to have a vascular or endocrine condition as a driver for the early onset of their disease. Conversely, 23% of those with ucHTN had a potential secondary cause of hypertension on MRI, even though their persistently high BP could be attributed to insufficient pharmacotherapy and these patients would not necessarily be considered to be at higher risk of secondary hypertension.

MRI is widely regarded as the gold standard non-invasive technique for assessing left ventricular volumes and mass(4), and also provides information about systolic and diastolic cardiac function(9). Whilst ECG is widely available as a screening tool, it has a relatively low sensitivity for LVH, particularly in those with obesity(23, 24). MRI is also superior to echocardiography for the assessment of LVM(25-27) (see Supplementary Table 1 for data on the accuracy of diagnosis of LVH using ECG or echocardiography versus CMR). The European Guidelines do not place much emphasis on myocardial dysfunction as a marker of target organ damage(2), however in this study 14% of patients had reduced ejection fraction and 42% had impaired long-axis function; ejection fraction

was generally preserved in our cohort, but using this parameter alone may miss significant cardiac systolic dysfunction in the presence of LVH(28).

MRI can also be used to characterize any change in the geometry of the left ventricle. Patients with normal range LVM, but concentric left ventricular remodeling are at increased cardiovascular risk compared with those with normal left ventricular mass and structure(29). The other additional advantage of MRI is the ability to evaluate replacement fibrosis using late gadolinium enhancement(30); in this study 5/15 myocardial infarctions seen on MRI were unexpected diagnoses and resulted in initiation of secondary prevention medication. Accurate evaluation of LVM, morphology and fibrosis also helps to differentiate between hypertensive heart disease and hypertrophic cardiomyopathy, which makes MRI an important tool for assessing patients with significant LVH and concurrent hypertension(6, 14, 31, 32). The use of gadolinium as an MRI contrast agent carries a risk of nephrogenic systemic fibrosis (NSF), quantified as an incidence of 0.02% in one retrospective, multicentre study of 83121 patients(33). Those with an estimated glomerular filtration rate of <30 ml/min/1.73m² are at highest risk of NSF (34). Novel techniques MRI techniques provide even more additional information; T1 mapping can quantify diffuse interstitial fibrosis (35, 36) and wave intensity analysis can be used to assess vascular stiffness(37). Table 4 summarises the comparison between different investigation modalities for the evaluation of LVH.

MRI is also a useful diagnostic tool for identifying potential secondary causes of hypertension (31). Renal artery stenosis was identified in 5% of our study population, but has been reported in as many as 24% of patients with resistant hypertension (38). European guidelines recommend duplex ultrasound as the first line investigation for RAS(2). This technique is non-invasive, but ultrasound can be limited by body habitus, does not penetrate air from bowel gas, and is not the 'gold-standard' examination for excluding RAS. Duplex ultrasound is also highly operator dependent with a sensitivity of 75% and specificity of 89.6% in experienced hands(39). More robust alternatives are therefore CT angiography and gadolinium-enhanced MR angiography (MRA). CT angiography has

excellent spatial and temporal resolution with a sensitivity of 94% and specificity of 93% for detecting RAS(39), however, CT angiography exposes patients to ionizing radiation and requires the use of an iodinated contrast agent, with a risk of contrast induced nephropathy in patients with renal impairment(40). Gadolinium-enhanced MRA, as used in this study, has now become much more widely available and has a similar sensitivity and specificity to CT angiography (90% and 94.1% respectively), although does carry a very small risk of NSF in patients with renal impairment as described above.

Adrenal masses and hyperplasia can be detected using MRI, however the frequent occurrence of incidental adrenal masses, commonly non-active adenomas, means that biochemical assessment should be the primary screening tool for endocrine hypertension(31). Our MRI protocol includes a simple single breath-hold axial T1-weighted imaging stack (5mm slice thickness) through the abdomen to screen for 'resolvable' adrenal lesions and so small abnormalities may be missed. High resolution adrenal CT or MRI, beyond our study protocol, is therefore required in patients with positive biochemistry to identify microadenomas and differentiate between pheochromocytomas and adenomas presenting as Conn's or Cushing's syndrome(6, 31). Pituitary lesions can be seen on standard MRI, however, a dedicated, contrast-enhanced MRI scan is also required to localize pituitary microadenomas(6).

In this study only 2/12 adrenal masses were hormonally active and only 2/10 cases of renal artery stenoses went on to be stented. Furthermore, following initial investigation with MRI further imaging was recommended in 12% of patients (see Table 3). Did these other findings and investigations generate unnecessary patient stress or healthcare costs?

Incidental findings may be identified via any imaging modality, however it is more likely when performing cross-sectional imaging of large areas of the body as seen with MRI and CT. The patients in this study were already undergoing assessment for secondary hypertension with concurrent

endocrine testing, we were therefore able to interpret any adrenal abnormalities in the context of the patient's endocrine profile, and so in clinical practice we have found these investigations to be complimentary. On the other hand, patients with 'normal' adrenals on MRI but a positive endocrine diagnosis would in practice require additional, high resolution focused adrenal imaging.

RAS is a recognised cause of hypertension(38), however the management of RAS has become controversial following data from studies, including the ASTRAL and CORAL trials, which showed no benefit of renal artery stenting over medical management with renin-angiotensin system blockade(41, 42). The picture has been further complicated by the advent of renal denervation; assessment of renal artery anatomy is used to screen for suitability for this interventional treatment for hypertension(43, 44).

Finally, other incidental findings may have both positive and negative impacts on patients. For example, the novel finding of a bicuspid aorta valve means that patients can be put under surveillance for significant valvular dysfunction or aortopathy, and whilst this may well create additional anxiety, early identification of these issues may prevent serious complications. In light of these concerns, we would emphasise that MRI is best targeted at those patients in which the increased likelihood of target organ or secondary causes of hypertension can justify the impact of any incidental findings.

Limitations

This study is a retrospective analysis of prospectively gathered clinical MRI data; as such we have no control group, and therefore cannot comment on the prevalence of target organ damage or secondary hypertension found on imaging in comparison with a normotensive population.

Additionally, we are unable to present a comparison between our MRI data and baseline data acquired using more conventional investigation techniques across our full cohort, and where comparisons were made with other imaging modalities, the data was in the form of non-

standardised clinical reports. There was also a proportion of patients seen in the hypertension clinic in which MRI was not indicated (especially if previously investigated), and patients who were not referred for MRI due to a history of claustrophobia, metal foreign body or implant, or morbid obesity meaning that their girth was too large for the MRI scanner; this may represent a selection bias. We clearly recognise that this is a skewed population of hypertensive patients who have been referred for further assessment in a specialist clinic, and these data cannot be extrapolated to the general hypertensive population who are routinely managed in primary care.

Finally, **the cost of MRI and access to this imaging modality can be extremely variable.** We acknowledge that no formal cost-benefit analysis has been performed for MRI assessment versus echocardiography and renal ultrasound/CT in this cohort (the approximate costs of these different investigations are shown in Supplementary Table 2). Existing data indicates that there may be a cost-benefit of echocardiography over ECG in the diagnosis of LVH in selected populations, but there is little formal data on any potential cost-benefit of MRI vs standard techniques and further research is required(45, 46).

Conclusions

MRI is a safe and effective imaging modality for screening patients with high blood pressure for asymptomatic target organ damage and secondary causes of hypertension. It provides high diagnostic specificity and sensitivity for identifying left ventricular hypertrophy and renal artery stenosis, and whilst CMR is not one of the primary imaging modalities recommended in clinical hypertension guidelines(2), it is the current gold standard for the non-invasive assessment of left ventricular volumes, mass and function(6, 31). We acknowledge that MRI remains a relatively expensive investigation and is not routinely available in the community, however diagnostic information from multiple organ systems can be obtained from a one hour scanning session, and this increased efficiency will be of benefit to patients. Target organ damage was identified in >75% of our

study population, resulting in the initiation of secondary prevention medication in those with newly identified cardiovascular disease, and triggering the initiation of anti-hypertensive medication in many of those with young onset hypertension. Given the high prevalence of target organ damage reported in this study and the clinical impact of our findings, we recommend that MRI should be used as the primary imaging modality in tertiary hypertension clinics.

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Figure Legends

Figure 1. MRI of target organ damage in hypertension. **A.** Left ventricular mid-cavity steady state free precession (SSFP) short-axis cine image at end-diastole (Ai) left-ventricular 4-chamber / horizontal long-axis SSFP cine image at end-diastole (Aii) images from the same patient showing elevated indexed left ventricular mass consistent with left ventricular hypertrophy. **B.** Left ventricular mid-cavity SSFP cine image at end-diastole from another patient demonstrating left ventricular hypertrophy (Bi) LV short-axis mid-cavity magnitude inversion recovery myocardial late gadolinium enhancement image showing evidence of patchy mid-wall replacement myocardial fibrosis (Bii, indicated by arrow) – these findings raises the possibility of previously undiagnosed hypertrophic cardiomyopathy in this case. **C&D.** Phase Sensitive Inversion Recovery (PSIR) images showing late gadolinium enhancement of (C) a lateral, subendocardial infarction and (D) an infero-lateral (circumflex territory), subendocardial infarction (indicated by arrows).

Figure 2. Secondary causes of hypertension demonstrated on MRI. **A.** Maximal intensity, arterial phase, coronal image (TWIST-MR angiography) showing left ostial renal artery stenosis (indicated by arrow) with left accessory renal artery inferior to main renal artery. **B.** TWIST-MRA showing right accessory renal artery (incidental finding, indicated by arrow). **C.** Single left mal-rotated and inferiorly positioned kidney in a patient with renal coloboma syndrome (delayed phase coronal image from TWIST-MRA showing arterial and venous phase imaging). **D.** Multiple hypo-attenuating, well-defined entities in both renal cortices on nephrographic phase imaging from coronal TWIST-MRA, which represent renal cysts in a patient with polycystic kidney disease (see arrows). **E.** Maximum intensity projection sagittal image showing coarctation of the aorta just distal to the left

subclavian artery (marked by arrow) and numerous collateral vessels (starred). **F.** Right benign adrenal nodule (see arrow). **G.** Bilateral adrenal phaeochromocytomas in a patient with multiple endocrine neoplasia type IIa (see arrows). **H.** Large left thyroid nodule (see arrow). F, G and H are axial HASTE images.

Tables

Parameter	All Patients (n=200)	Patient Hypertension Subgroups			
		Drug Resistant (n=76)	Young Onset (n=64)	Uncontrolled (n=35)	Other* (n=25)
Age (years)	51 ± 15	58 ± 10	35 ± 9	65 ± 9	53 ± 10
Gender (no. male)	115 (56%)	46 (61%)	37 (58%)	17 (49%)	15 (60%)
BMI (kg/m ²)	30 ± 6	31 ± 5	29 ± 7	29 ± 5	31 ± 6
No. anti-hypertensives	3.1 ± 2.0	4.8 ± 1.5	1.9 ± 1.5	2.0 ± 1.3	2.2 ± 1.3
SBP (mmHg)	168 ± 30	178 ± 29	152 ± 22	187 ± 27	154 ± 23
DBP (mmHg)	96 ± 16	99 ± 17	94 ± 11	100 ± 16	91 ± 16
LVM (g/m ²)	87 ± 28	96 ± 31	78 ± 24	83 ± 21	87 ± 29

Table 1. Patient demographics, by hypertension subgroup. BMI, body mass index; SBP, systolic

blood pressure; DBP, diastolic blood pressure; LVM, left ventricular mass indexed to body surface

area. *Includes patients with accelerated hypertension, highly labile hypertension, or hypertension with disproportionate target organ damage warranting further investigation.

Parameter	All Patients (n=200)	Patient Hypertension Subgroups				
		Drug Resistant (n=76)	Young Onset (n=64)	Uncontrolled (n=35)	Other* (n=25)	P value
Target organ damage, n (%)	157 (79)	70 (92)	38 (59)	31 (89)	18 (72)	<0.0001
Left ventricular hypertrophy, n (%)	122 (61)	56 (74)	24 (38)	26 (74)	16 (64)	<0.0001
Secondary causes, n (%)	29 (15)	13 (17)	4 (6)	8 (23)	7 (28)	=0.04

Table 2. Prevelence of all types of target organ damage, left ventricular hypertrophy and potential secondary causes of hypertension identified on MRI, with comparison by hypertensive subgroups.

*Includes patients with accelerated hypertension, highly labile hypertension, or hypertension with disproportionate target organ damage warranting further investigation.

Pathology	No. cases	Details
Adrenal mass	12	<ul style="list-style-type: none"> 7 lesions were not hormonally active. <ul style="list-style-type: none"> 1 reported as a likely pheochromocytoma on MRI, but non-functional adenoma following endocrine testing and dedicated adrenal CT. 1 patient with bilateral pheochromocytomas and a thyroid nodule diagnosed with multiple endocrine neoplasia type 2a, now under oncological treatment. 1 patient had a resolution of their hypertension following treatment with spironolactone. 3 patients have not had endocrine pathology excluded <ul style="list-style-type: none"> 1 died of a stroke prior to investigation 1 emigrated prior to full investigation 1 is still under investigation
Renal artery stenosis	10	<p>Cases reviewed at renal multidisciplinary team meeting:</p> <ul style="list-style-type: none"> 2 referred for stenting 8 for medical management
Renal abnormality	21	<p>6/21 findings may reflect secondary hypertension:</p> <ul style="list-style-type: none"> 2 atrophy secondary to RAS 2 atrophy not related to RAS 1 polycystic kidney disease; consistent with family history of the condition. 1 single hypoplastic, malrotated kidney in keeping with previous diagnosis of renal coloboma syndrome (autosomal dominant condition characterised by renal hypodysplasia, optic nerve dysplasia and hypertension)(47) <p>15/21 findings likely incidental:</p>

		<ul style="list-style-type: none"> • 9 uni- or bilateral simple cyst(s) • 4 anatomical variants not felt to cause hypertension (e.g. horseshoe kidney and duplex malrotated kidney) • 1 patient with pelvicalyceal dilatation and possible renal parenchymal abnormality; further defined on CT and felt to be benign. • 1 previous nephrectomy for loin pain haematuria syndrome. <ul style="list-style-type: none"> – Not known to cause hypertension(48); referral for renal denervation to treat concurrent resistant hypertension and, potentially, loin pain(49, 50).
Thyroid abnormality	7	Goitre and nodules; assessed biochemically and referred further investigation if indicated. 1 case MEN2a see above.
Pituitary enlargement	1	Investigated with pituitary function testing and a pituitary MRI; non-functional.
Aortic coarctation	1	Associated with bicuspid aortic valve and aortopathy. Novel diagnosis, hypertension resolved following endovascular stenting.
<i>Incidental findings</i>		<i>3 bicuspid aorta valves (now on surveillance), 1 pulmonary nodule, 2 splenomegaly, 1 liver lesion (haemangioma), gallstones, uterine fibroids, and breast, liver, pancreatic and renal cysts.</i>

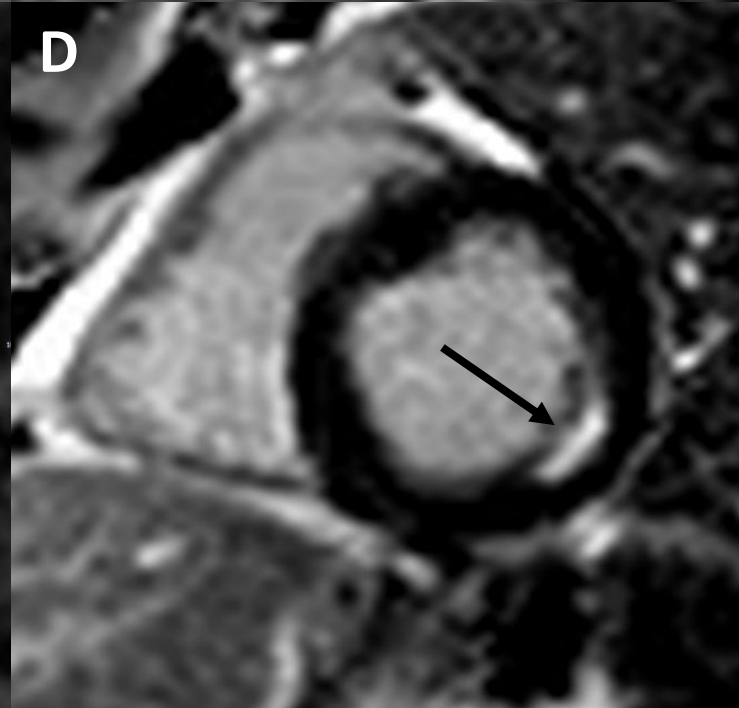
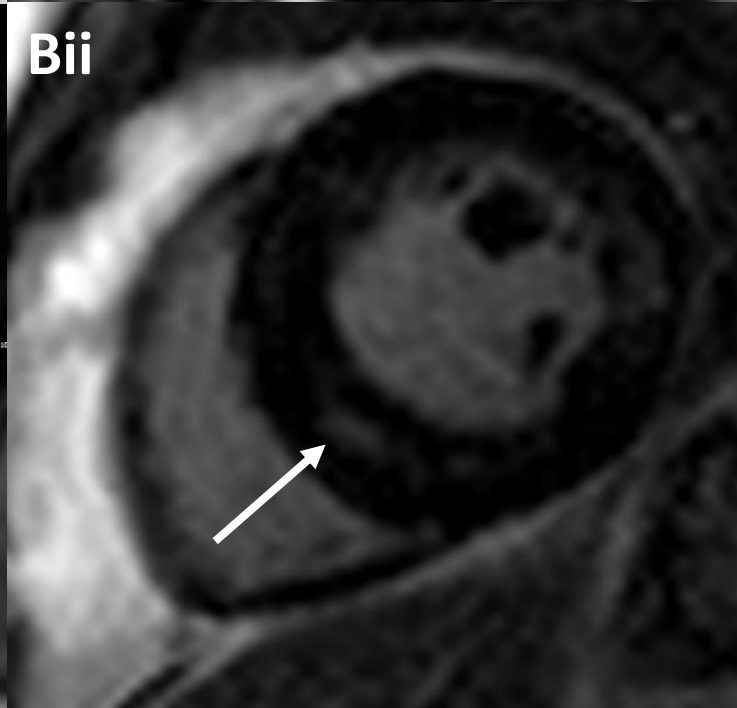
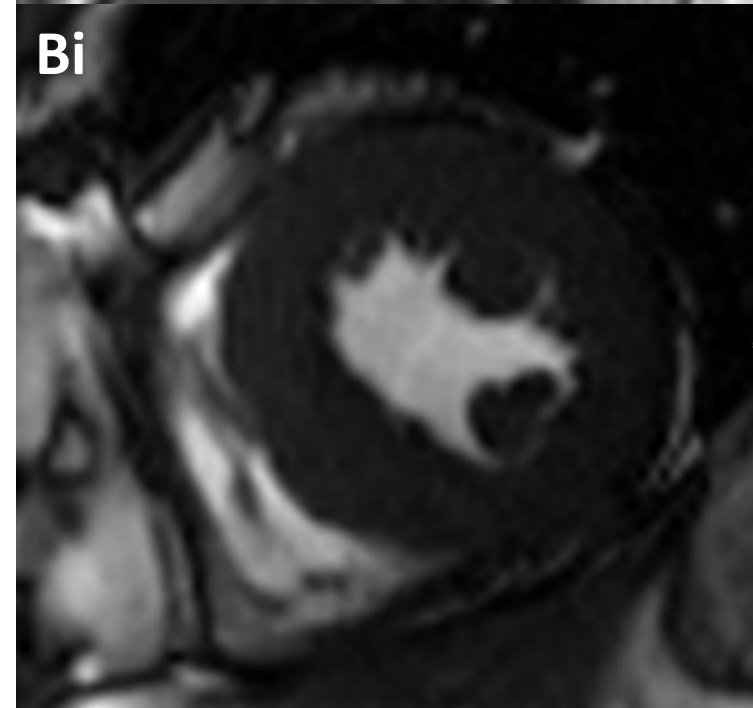
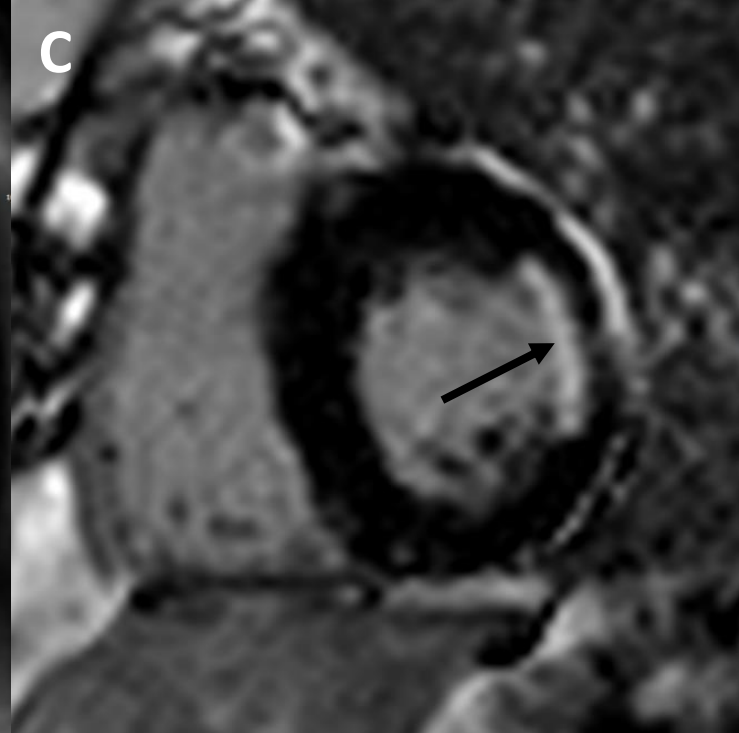
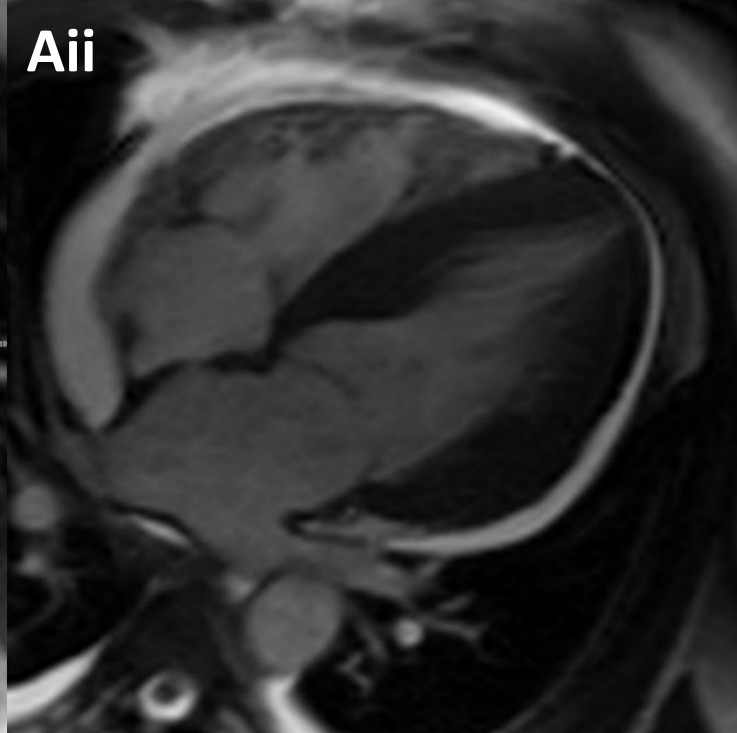
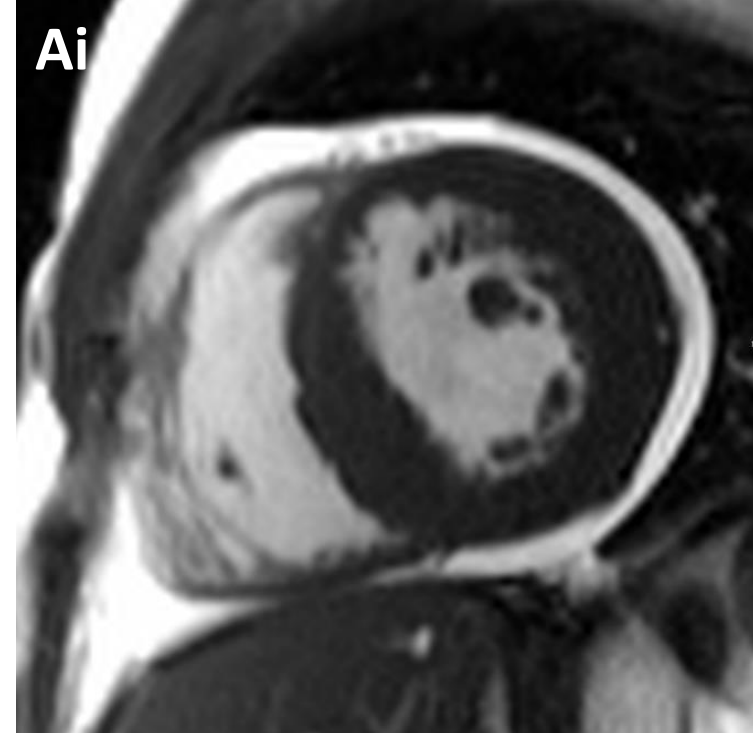
Table 3. Secondary causes of hypertension, and other incidental findings, as demonstrated by MRI.

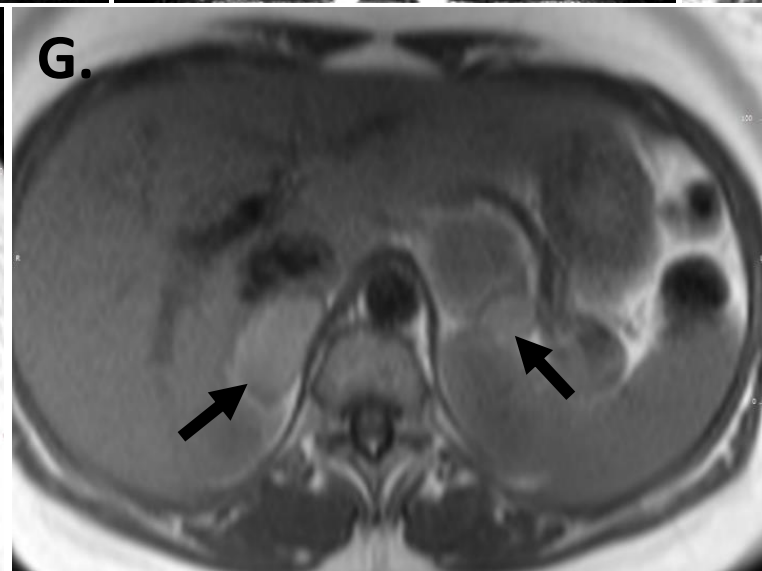
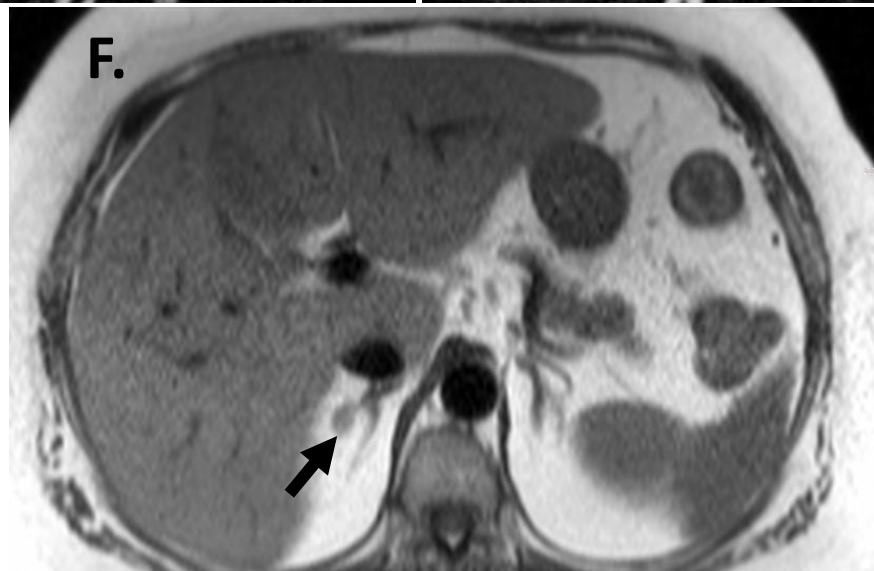
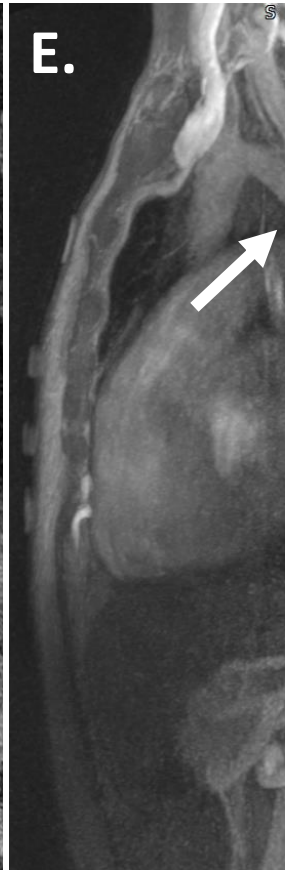
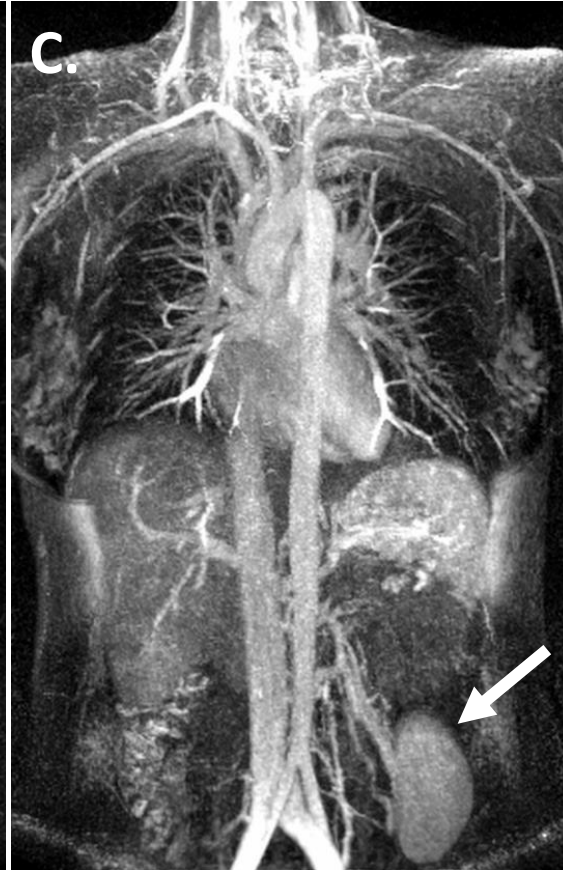
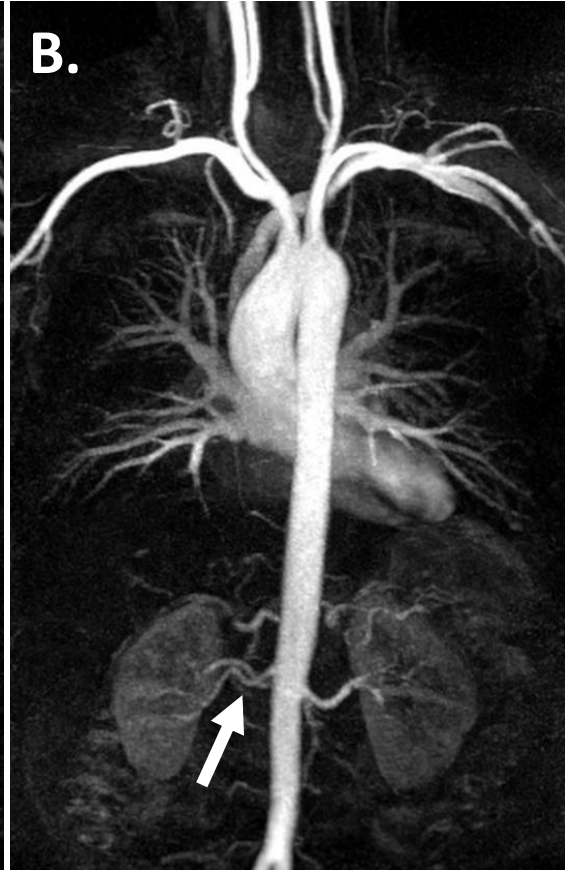
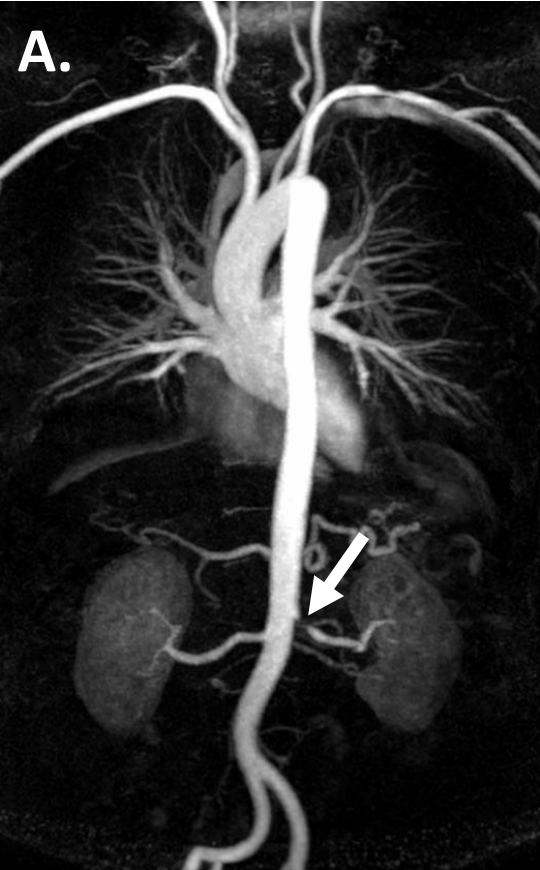
RAS, renal artery stenosis.

Investigation	Benefits	Limitations	Supporting references
Electrocardiogram	<ul style="list-style-type: none"> • Safe, cheap and accessible. • Prognostic data. 	<ul style="list-style-type: none"> • Low sensitivity for LVH, especially in obesity. 	Cuspidi et al. 2014(51) Bacharova et al. 2015(23) Rodrigues et al. 2016(24)
2D Echocardiography	<ul style="list-style-type: none"> • Safe, low cost and widely available. • Good sensitivity for LVH and significant myocardial infarction. • Prognostic data. 	<ul style="list-style-type: none"> • Images can be limited by body habitus. • Geometrical assumptions made for the quantification of LV volumes. 	Levy et al. 1990(52) Verdecchia et al. 2001(53) Myerson et al. 2002(25)
3D Echocardiography	<ul style="list-style-type: none"> • Safe. • Similar accuracy for estimation of LVM to CMR. 	<ul style="list-style-type: none"> • Specialist equipment and trained operators required with limited availability. 	Nosir et al. 1998(54) Kuhl et al. 2000(55)
Cardiac CT	<ul style="list-style-type: none"> • Multiple images slices attained in a single breath hold. • Reasonable accuracy. • Prognostic data. 	<ul style="list-style-type: none"> • Exposure to ionizing radiation and requires intravenous contrast agent. 	Mousseaux et al. 1994(56) Klein et al. 2016(57)
CMR	<ul style="list-style-type: none"> • Safe, non-ionising. • Superior accuracy and reproducibility for the quantification of LVM compared with 2D echocardiography. • Late gadolinium enhancement assesses fibrosis/scar. • Helpful to define aetiology of LVH. • Prognostic data. • Can reduce sample size in research studies. 	<ul style="list-style-type: none"> • Limited accessibility outside specialist centres, high cost. • Contraindicated for device implants, cerebral clips, claustrophobia, etc. • Possible incidental findings. • Risk of nephrogenic sclerosing fibrosis in patients with significant renal impairment. 	Bottini et al. 1995(27) Bellenger et al. 2000(58) Grothues et al. 2002(59) Myerson et al. 2002(4) Chirinos et al. 2010(60)

Table 4. Comparison between different investigation modalities for the evaluation of left

ventricular hypertrophy. CT, computerised tomography; CMR, cardiac magnetic resonance; LVH, left ventricular hypertrophy; LVM, left ventricular mass.





Supplementary Data

Imaging modality	Cohort size (n=)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	References
Electrocardiogram						
- Sokolow–Lyon voltage	128	19	93	60	66	Rodrigues et al. 2016, Hypertensives(1)
- Sokolow–Lyon product	128	17	96	72	66	Rodrigues et al. 2016, Hypertensives(1)
- Cornell voltage	128	43	84	61	72	Rodrigues et al. 2016, Hypertensives(1)
- Sokolow–Lyon and/or Cornell voltage	4748	16	95	35	87	Bacharova et al. 2015, Multi-ethnic study of atherosclerosis(2)
- Sokolow–Lyon voltage	228	29	92	-	-	Alfakih et al, 2004, Hypertensives(3)
- Sokolow–Lyon product	228	37	91	-	-	Alfakih et al, 2004, Hypertensives(3)
- Cornell voltage	228	21	95	-	-	Alfakih et al, 2004, Hypertensives(3)
- Cornell product	228	31	91	-	-	Alfakih et al, 2004, Hypertensives(3)
2D Echocardiography						
	84	79	68	77	70	<i>This study cohort, 2016 Hypertensives</i>
	80	86	85	55	97	Jackubovic et al, 2013 Dialysis/controls(4)

Supplementary Table 1: Examples of sensitivities, specificities and predictive values for the diagnosis of left ventricular hypertrophy by different techniques versus cardiac magnetic resonance (CMR). PPV, positive predictive value; NPV, negative predictive value.

1. Rodrigues JC, McIntyre B, Dastidar AG, Lyen SM, Ratcliffe LE, Burchell AE, et al. The effect of obesity on electrocardiographic detection of hypertensive left ventricular hypertrophy: recalibration against cardiac magnetic resonance. *J Hum Hypertens.* 2016;30(3):197-203.
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3. Alfakih K, Walters K, Jones T, Ridgway J, Hall AS, Sivananthan M. New gender-specific partition values for ECG criteria of left ventricular hypertrophy: recalibration against cardiac MRI. *Hypertension.* 2004;44(2):175-9.
4. Jakubovic BD, Wald R, Goldstein MB, Leong-Poi H, Yuen DA, Perl J, et al. Comparative assessment of 2-dimensional echocardiography vs cardiac magnetic resonance imaging in measuring left ventricular mass in patients with and without end-stage renal disease. *Can J Cardiol.* 2013;29(3):384-90.

Imaging Modality	Cost, USD (GBP)
Echocardiogram	\$ 120 (£80)
Renal ultrasound	\$ 75 (£50)
CT angiogram – renal	\$ 135 (£90)
Complex CT – e.g. adrenal imaging	\$ 670 (£450)
Hypertension MRI	\$ 600 (£400)

Supplementary Table 2: Costs for different imaging modalities. These prices represent the current cost of these investigations at our Institution and are given for reference, however prices will show considerable geographical variation. Conversion from Great British Pounds (GBP) to United States Dollars (USD) correct June 2016.